

Compensation in Safeguarding Children: Pediatric Medical Countermeasure Research

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I. Introduction

In its report, *Safeguarding Children: Pediatric Medical Countermeasure Research* (*Safeguarding Children*), the Presidential Commission for the Study of Bioethical Issues (Bioethics Commission) advised the U.S. government on the ethical considerations involved in evaluating and conducting pediatric medical countermeasure research both before a bioterrorism attack (pre-event) and after an attack (post-event). The Bioethics Commission's analysis included specific consideration of anthrax vaccine adsorbed (AVA), a vaccine that would be made available for post-event prophylaxis in the event of an anthrax attack.

The term medical countermeasure (MCM) has been defined in different ways. In *Safeguarding Children*, the Bioethics Commission considered it to include U.S. Food and Drug Administration (FDA)-regulated products and interventions used in response to chemical, biological, radiological, and nuclear attacks.¹ In *Safeguarding Children*, the Bioethics Commission

¹ Presidential Commission for the Study of Bioethical Issues (PCSB). (2013, March). *Safeguarding Children: Pediatric Medical Countermeasure Research*. Washington, DC: PCSBI, p. 18.

considered the ethical obligation to treat or compensate participants injured as a result of participating in pediatric MCM research.²

II. Learning Objectives

Students should be able to:

1. Discuss the ethical principles that give rise to an obligation to provide treatment or compensation for research related-injuries that arise from pediatric MCM research.
2. Describe the different arguments for treating or compensating injured adults versus injured pediatric research participants.
3. Describe the different ways that injured pediatric MCM research participants can obtain treatment or compensation and the strengths and limitations of these approaches.

III. Background

In *Safeguarding Children*, the Bioethics Commission considered compensation for research-related injury in the context of pediatric MCM research. Compensation for research-related injury is an established practice in most developed countries, excluding the United States, in which sponsors, investigators, or others engaged in research provide treatment or compensation when injuries arise.³ In *Safeguarding Children*, the Bioethics Commission reaffirmed the conclusion that it reached in *Moral Science: Protecting Participants in Human Subjects Research*—that participants “harmed in the course of human subjects research ought not individually bear the costs of care required to treat qualified harms resulting directly from that research.”⁴

A. Guiding Ethical Principles

Pediatric MCM researchers have an ethical obligation to protect participants from the physical and financial harms that can result from research participation. In pediatric MCM research, fulfilling this ethical obligation requires that researchers have a plan in place to treat or compensate injured research participants.

² Throughout this module, the terms “treatment” and “compensation” are used in ways that reflect Bioethics Commission usage or the language of particular institutional policies. Treatment refers generally to medical treatment provided in response to a research-related injury, whereas compensation refers to financial payments made following a research-related injury.

³ Presidential Commission for the Study of Bioethical Issues. (2011, December). *Moral Science: Protecting Participants in Human Subjects Research*. Washington, DC: PCSBI, p. 24.

⁴ Ibid, p. 62.

This obligation is grounded in several ethical principles including justice, beneficence, and respect for persons. One theory of justice suggests that the benefits and burdens of research should be distributed equitably (i.e., that no person involved in research should be disproportionately burdened as a result of their participation).⁵ Justice therefore requires that children who participate in pediatric MCM research—accepting certain risks to generate knowledge that is more likely to benefit other children or society generally—be protected against bearing disproportionate physical or financial harms.⁶ Researchers protect participants from harm in a number of ways, including by minimizing risk, providing an informed consent process, and subjecting proposed research to institutional review board review. Providing medical treatment and financial compensation is a way of protecting participants from bearing a disproportionate share of the burden.

The principles of beneficence and respect for persons both call for taking action to reduce risks to research participants. Beneficence calls on researchers to ensure the wellbeing of research participants; the corollary principle, non-maleficence, requires minimizing the harms that are imposed.⁷ Respect for persons requires respecting individuals as capable of making autonomous decisions and establishes that persons with diminished capacity, such as children, are entitled to additional protections.⁸ Because children cannot legally or ethically consent to participate in research and accept risks for the benefit of others, additional protections such as compensation for research-related injury are particularly warranted. Respect for persons similarly requires not exposing participants to unnecessary risks—including the risks of unnecessary physical and financial harms that can result from research. In accordance with the principles of beneficence and respect for persons, providing treatment and compensation for research-related injury is one way that risks to participants can be minimized.⁹

B. Legal Background

Federal regulations governing protection of research participants have been codified by the U.S. Department of Health and Human Services in the Code of Federal Regulations at 45 C.F.R. Part 46 (Subpart A of which is often referred to as the Common Rule). The Common Rule

⁵ PCSBI, (2011, September), op cit, p. 63; The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1977). *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects Research* (DHEW Publication OS 78-0012). Washington, DC: Department of Health, Education, and Welfare.

⁶ PCSBI, (2013, March), op cit, p. 76.

⁷ Presidential Commission for the Study of Bioethical Issues. (2013, December). *Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts*. Washington, DC: PCSBI, p. 4; Resnik, D.B. (2006). Compensation for research-related injuries: Ethical and legal issues. *Journal of Legal Medicine*, 27, 263-287; The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1977). *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects Research* (DHEW Publication OS 78-0012). Washington, DC: Department of Health, Education, and Welfare.

⁸ PCSBI, (2013, March), op cit, p. 25.

⁹ Ibid, p. 76.

establishes general requirements for informed consent including, but not limited to, explanation of the research study, description of expected benefits and potential risks, explanation of confidentiality, and a statement of voluntariness specifying that participants can withdraw from the study at any time with no penalty.¹⁰ The Common Rule does not require that compensation or any medical treatments actually be provided in the event of a research-related injury, however it requires that for research involving more than minimal risk, an explanation be provided about “whether any compensation [or] any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.”¹¹

Additional protections for research involving children are codified at 45 C.F.R. 46, Subpart D. These regulations limit the level of research risk to which pediatric research participants can be exposed.¹² They do not, however, require that compensation be provided in the event of a research-related injury.

In the context of MCMs, injured research participants might find additional protection in the Public Readiness and Emergency Preparedness (PREP) Act, a law that provides some compensation for those injured as a result of receiving an MCM.¹³ The PREP Act provides compensation for those who suffer “serious physical injury or death” and who bring claims for their injury within one year.¹⁴ It is not clear, however, whether Congress will appropriate funds for this purpose.¹⁵

If the MCM under consideration is a vaccine listed in the Vaccine Injury Table, injured research participants might be eligible for compensation under the National Vaccine Injury Compensation Program (U.S. Vaccine Court).¹⁶ The U.S. Vaccine Court is the primary mechanism by which those injured after receiving a vaccine receive compensation.¹⁷

C. Bioethics Commission Recommendations

Two of the Bioethics Commission’s six recommendations in *Safeguarding Children* address treatment or compensation for research-related injury.

¹⁰ *Protection of Human Subjects*, HHS. 45 C.F.R. § 46.116.

¹¹ *Protection of Human Subjects*, HHS. 45 C.F.R. § 46.116(a)(6).

¹² *Protection of Human Subjects*, HHS. 45 C.F.R. Subpart D.

¹³ PCSBI, (2013, March), op cit, p. 78.

¹⁴ *PREP Act*. 42 U.S.C. §§ 247d-6d(i)(1).

¹⁵ *Countermeasures Injury Compensation Program (CICP): Administrative Implementation*, HHS. 42 C.F.R. Part. 110.

¹⁶ The Office of Special Masters, U.S. Court Of Federal Claims. (2004). Guidelines for Practice Under The National Vaccine Injury Compensation Program. Retrieved August 15, 2014 from <http://www.uscfc.uscourts.gov/sites/default/files/OSM.Guidelines.pdf>.

¹⁷ PCSBI, (2013, March), op cit, p. 77.

Recommendation 4: Ethical Framework for National-Level Review of Pre-event Pediatric Medical Countermeasure Research [excerpt]

To ensure the thoroughness and ethical rigor of national-level review, reviewers should apply the Bioethics Commission's recommended ethical framework for reviewing pre-event pediatric medical countermeasure research that poses greater than minimal risk, but no more than a minor increase over minimal risk, under Department of Health and Human Services regulations at 45 C.F.R. § 46.407 and/or U.S. Food and Drug Administration regulations at 21 C.F.R. § 50.54. A proposed protocol must meet the requirements of the framework outlined in this report to be approved.

The framework also specifies a rigorous set of conditions necessary to determine whether the research would be conducted in accordance with the required "sound ethical principles" [including]...post-trial requirements to ensure ethical distribution of medical countermeasures in the event of an attack, as well as a plan for treatment or compensation for research-related injury...¹⁸

Recommendation 5: Post-event Pediatric Medical Countermeasure Research

Post-event research should be planned in advance and conducted when untested medical countermeasures are administered to children in an emergency or when limited pre-event medical countermeasure studies have already occurred. Institutional review boards must be cognizant of the exigencies imposed upon research under emergency conditions, and when reviewing post-event medical countermeasure research proposals, ensure that adequate processes are in place for informed parental permission and meaningful child assent. Institutional review boards must also ensure that the research design is scientifically sound, children enrolled in research have access to the best available care, adequate plans are in place to treat or compensate children injured by research, and provisions are made to engage communities throughout the course of research.¹⁹

IV. Reading

For the purposes of discussion, students should download and read the following Bioethics Commission materials (reports are available for download on the Bioethics Commission's website at www.bioethics.gov under "Projects"):

Safeguarding Children: Pediatric Medical Countermeasure Research, pp. 76-78
("Compensation for Research-Related Injury").

¹⁸ PCSBI, (2013, March), op cit, p. 6.

¹⁹ Ibid, pp. 7-8.

Compensation for Research-related Injury Background, pp. 2-17 (“Introduction” and “Background”).

V. Discussion Questions

The following questions are based on the information provided above and through the indicated reading and are intended to reinforce important aspects of compensation for research-related injury that are highlighted in *Safeguarding Children*. Important points are noted with each question to help the instructor guide a group discussion. The “Additional Resources” section is a helpful source in answering these questions.

1. What ethical principles support treating or compensating pediatric participants injured as a result of participating in MCM research?

Starting points for discussion:

- a. The ethical principal of justice supports providing medical treatment or compensation to injured pediatric MCM research participants as a way of ensuring that these injured research participants do not bear a disproportionate share of the burdens of research.
- b. The ethical principles of beneficence and respect for persons require that risks to pediatric participants be minimized; in this context, providing medical treatment or compensation for research-related injury helps minimize the additional harm that can result from research-related injuries in accordance with these principles.

2. What distinguishes pediatric research participants from adult research participants, and how might that lead to different arguments for treating or compensating injured research participants?

Starting points for discussion:

- a. Adults are able to provide ethically and legally valid informed consent prior to participating in research. Some argue that adult research participants are therefore able to assume the risks of research through the informed consent process.
 - i. However, the informed consent process is not a voluntary assumption of risks; rather, it is intended to protect research participants and ensure that decisions to participate in research are voluntary and uncoerced. An agreement to participate in research that acknowledges risks is different than agreeing to assume the physical and financial burdens should those risks come to pass.
 - ii. In addition, certain risks might be unknown or unforeseen at the time consent was given. Research participants cannot reasonably be thought to have

knowingly and voluntarily accepted risks that were unknown or unforeseen at the time they gave consent.

- b. By contrast, pediatric research participants are unable to legally or ethically consent to participate in research, and therefore cannot fully accept the risks of research in the same way that adult research participants might be able to. This weakens any claim that pediatric research participants have waived their claim to care or compensation for research-related injuries by agreeing to participate.

3. In what ways is the Bioethics Commission's compensation recommendation in *Safeguarding Children* similar to that made in *Moral Science: Protecting Participants in Human Subject Research*? In what ways is it different?

The following additional reading might be useful in considering this question:

Moral Science: Protecting Participants in Human Subjects Research, pp. 56-70
("Treating and Compensating for Research-Related Injury").

Starting points for discussion:

- a. In *Safeguarding Children*, the Bioethics Commission reaffirmed its previous conclusion, noted in *Moral Science*, that "subjects harmed in the course of human subjects research ought not individually bear the costs of care required to treat qualified harms resulting directly from that research." (77)
- b. In *Moral Science*, the Bioethics Commission recommended further study of the issue.
- c. In *Safeguarding Children*, the Bioethics Commission made two more specific recommendations.
 - i. It recommended that all children who enroll in pre-event pediatric MCM research that is greater than minimal risk and less than a minor increase over minimal risk, and become injured as a result of their participation, should be guaranteed all necessary medical care or appropriate compensation for such injuries.
 - ii. The Bioethics Commission also recommended that, in post-event pediatric MCM research, IRBs ensure that adequate plans are in place to treat or compensate children injured by research.

VI. Problem-Based Learning

Scenario A. *A researcher conducting pediatric MCM research is meeting with parents who are considering enrolling their child in the study. The parents ask what might happen in the event that their child is injured as a result of the research.*

The following additional reading might be useful in considering this question:

Compensation for Research-related Injury Background, pp. 2-4 (“Why Compensate Injured Participants?”)

1. What information can the researcher provide to the family about avenues at the national level for receiving treatment or compensation for research-related injury?

Starting points for discussion:

- a. There is currently no overarching federal policy to ensure that injured research participants receive treatment or compensation.
- b. The U.S. Vaccine Court might provide some protection if the research involves a vaccine listed in the Vaccine Injury Table or recommended by the Centers for Disease Control and Prevention (CDC) for routine administration. However, the program provides no protection if the MCM being studied is not a listed vaccine.
- c. Provided that the injury is sufficiently serious and manifests within a year of receiving the MCM, the family might be able to receive compensation under the Covered Countermeasure Process Fund established by the PREP Act. It is not clear, however, whether Congress will appropriate funds for this purpose.

2. What other avenues might be available to them?

Starting points for discussion:

- a. Per the Bioethics Commission’s recommendations in *Safeguarding Children*, researchers are ethically obligated to assure a plan is in place to provide treatment or compensation for the research-related injuries that arise from pediatric MCM research.
- b. The researcher should consider specific provisions in the protocol that describe the compensation available in the event of a research-related injury. The researcher could also refer to the informed consent document to determine what treatment or compensation might be available for research-related injury.

Scenario B. *You are a researcher employed by a university and you are about to conduct pediatric MCM research that is sponsored by a pharmaceutical company. You agree that there is an ethical obligation to compensate participants injured as a result of their participation in pediatric MCM research and are presented with several options for language about compensation to include in an informed consent document.*

Approach 1: Decisions about payment for medical treatment for injuries relating to your participation in research will be made by the university and the pharmaceutical company sponsor on a case-by-case basis.

Approach 2: If you are injured during the study, the pharmaceutical company sponsor will pay any reasonable and necessary medical expenses that are charged to you and not paid by your insurance company. These expenses will only be paid if both you and your study doctor abide by the rules of the study. You will be responsible for paying any medical expenses not related to the study. There is no payment available for such things as lost wages, discomfort, or disability. You do not give up your legal rights by signing this consent.

Approach 3: The university will provide compensation for any injury that arises during the pediatric MCM trial.

1. What are the strengths and weaknesses of each approach?

Starting points for discussion:

a. Approach 1

Strengths: Allows the stakeholders to remain flexible and evaluate claims as they arise. Might permit the party most at fault to provide compensation in accordance with the principles of compensatory justice.

Weaknesses: This approach is relatively vague and leaves open the possibility that an injured research participant's need for medical care and compensation could fall through the cracks.

b. Approach 2

Strengths: This approach is far more specific than Approach 1 and enables participants to know what they can expect from which parties. Injured research participants can still file a tort lawsuit, even though there are barriers to succeeding.

Weaknesses: This approach limits payment to certain types of harm. Moreover, the terms “reasonable and necessary” are subject to interpretation.

c. Approach 3

Strengths: This approach is very protective of injured research participants.

Weaknesses: This approach subjects the university to a potentially limitless payout and does not specify that the injury has to be caused by the research.

2. Which approach would you choose and why? If you would make modifications to your chosen approach, which modifications would you make and why?

Starting points for discussion:

- a. One could choose Approach 2, for example, because it seemingly takes a middle-ground approach to specifying when medical care and compensation will be provided to injured research participants that is less extreme than Approach 1 or Approach 3.
- b. If Approach 2 is chosen, one could suggest that the approach be modified so as not to limit the categories of claims for which injured research participants can receive compensation (e.g., children who are injured as a result of their participation in pediatric MCM research might be entitled to receive compensation for a wider range of compensable injuries).

VII. Exercises

Exercise A. *Describe existing federal programs that provide treatment or compensation for research-related injuries, including the U.S. Vaccine Court and the PREP Act. The following resources provide useful information:*

Presidential Commission for the Study of Bioethical Issues. (2013, March). *Safeguarding Children: Pediatric Medical Countermeasure Research*. Washington, DC: PCSBI, pp. 76-78.

Health Resources and Services Administrations, HHS. (n.d.). National Vaccine Injury Compensation Program. Retrieved August 14, 2014, from <http://www.hrsa.gov/vaccinecompensation/index.html>.

PREP Act. 42 U.S.C. §§ 247d-6d(i)(1).

Liu, E.C. (2010, February). Pandemic Flu and Medical Biodefense Countermeasure Liability Limitation. Congressional Research Service. Retrieved August 15, 2014, from <http://www.fas.org/sgp/crs/misc/RS22327.pdf>.

Health Resources and Services Administration, HHS. (n.d.). Vaccine Injury Table. Retrieved August 15, 2014 from <http://www.hrsa.gov/vaccinecompensation/vaccinetable.html>.

1. **What is the U.S. Vaccine Court?**
2. **Is the U.S. Vaccine Court adequate in the context of MCM research? Why or why not?**
3. **How does the PREP Act protect children injured as a result of participating in MCM research?**
4. **Is the protection afforded by the PREP Act sufficient? What are the limitations of the Act?**

Exercise B. *A number of institutions—including government agencies that support and conduct research—have policies to provide some treatment or compensation for research-related injury. One federal agency provides short-term medical care, but not long-term medical care or financial compensation, to those injured as a result of research conducted at its facilities.*

1. **What are the strengths and limitations of this policy with regard to pediatric MCM research?**
2. **As a pediatric MCM researcher at this agency, what terms would you want included in your informed consent document to ensure that participants are adequately protected?**

VIII. Glossary of Terms

Autonomy: The capacity to direct the course of one's own life or to live according to one's own values and beliefs.

Beneficence: An obligation on the part of researchers to undertake efforts to maximize possible benefits and minimize potential harms to research participants.

Distributive justice: An ethical principle that calls for equitable distribution of benefits and burdens across society—for example, the benefits and burdens of biomedical research, or of technological advances.

Informed consent: The process of informing and obtaining permission from an individual before conducting medical or research procedures or tests.

In the research setting, this involves researchers educating prospective research participants about the risks and potential benefits of a proposed study and prospectively seeking their consent to participate.

Medical countermeasure (MCM): FDA-regulated products and interventions used in response to chemical, biological, radiological, and nuclear attacks.

Non-maleficence: An obligation on the part of researchers not to cause intentional harm to research participants.

Protocol: A plan for the conduct of a research project, including all aspects of the project from recruitment to obtaining informed consent to dissemination of results.

Respect for persons: Ethical principle requiring that individuals are treated as independent and self-determining (autonomous) agents and that persons with diminished autonomy are entitled to additional protections.

IX. Additional Resources

Countermeasures Injury Compensation Program (CICP). 42 C.F.R. Part 110.

Feinberg, K.R., Administrator of the Gulf Coast Claims Facility and Special Master of the September 11 Victim Compensation Fund. (2011). Presentation to the Bioethics Commission, November 16. Retrieved August 15, 2014, from <http://bioethics.gov/node/392> and <http://tvworldwide.com/events/bioethics/111116/>.

Fleischman, A.R., and L.K. Collogon. (2008). Research with children. In E.J. Emanuel, et al. (Eds.). *The Oxford Textbook of Clinical Research Ethics*, pp. 446-460. New York, NY: Oxford University Press.

Health Resources and Services Administrations, HHS. (n.d.). National Vaccine Injury Compensation Program [Webpage]. Retrieved August 18, 2014 from <http://www.hrsa.gov/vaccinecompensation/index.html>.

PREP Act. 42 U.S.C. §§ 247d-6d(i)(1).

Liu, E.C. (2010, February). Congressional Research Service: Pandemic Flu and Medical Biodefense Countermeasure Liability Limitation. Retrieved August 15, 2014, from <http://www.fas.org/sgp/crs/misc/RS22327.pdf>.

Resnik, D.B. (2006). Compensation for research-related injuries: Ethical and legal issues. *Journal of Legal Medicine*, 27, 263-287.

Steinbrook, R. (2006). Compensation for injured research subjects. *New England Journal of Medicine*, 354(18), 1871-1873.